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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/541,377	07/06/2005	Valerie Autier	MERCK-3028	8732

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EXAMINER	
HUGHES, ALICIA R	

ART UNIT	PAPER NUMBER
1614	

MAIL DATE	DELIVERY MODE
04/17/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/541,377	AUTIER ET AL.	
	Examiner	Art Unit	
	ALICIA R. HUGHES	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 December 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *16,27,28,30-39 and 44-46* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *16,27,28,30-39 and 44-46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

Claims 16, 27-28, 30-39 and 44-46 are pending and the subject of this Office Action.

Applicant's remarks filed on 01 December 2008 and 20 August 2008 have been fully considered and are deemed to be persuasive regarding the previous rejections made of record. Therefore, the finality of the Office Action issued on 29 May 2008 is hereby VACATED.

Rejections and objections not reiterated from previous office actions are hereby withdrawn. The following rejections are reiterated and expounded upon, and they constitute the complete set presently being applied to the instant application.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re*

Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 16, 27-28, 30-39 and 44-46 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-14, 28-29, 33, and 55-56 of U.S. Patent Application No. 10/541,493. Although the conflicting claims are not identical, they are not patentably distinct from each other, because they contain overlapping/closely related subject matter, most notably, the treatment of diabetes and related complications by administering to a patient in need thereof a kynurenine 3-hydroxylase inhibitor.

Applicant has noted that the '493 application does not teach or suggest the specific compounds in the present set of claims and therefore, the obvious-type double patenting rejection should be withdrawn. To the contrary, it is well-understood in art that an obvious-type double patenting rejection does not require anticipation, but rather, a show of a *prima facie* case of obviousness, which has been established based on the administration of a kynurenine 3-

hydroxylase inhibitor, and some with the same core structure as claimed in the instant application.

In view of the foregoing, the above rejection is proper.

Claim Rejections – 35 U.S.C. §103(a)

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office Action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 16, 27-28, and 30-46 are rejected under 35 U.S.C. §103(a) as being obvious over U.S. Patent No. 6,323,240 B1 [hereinafter referred to as "Giordani et al"] in view of U.S. Patent No. 6,572,542 [hereinafter referred to as "Houben et al"].

The teachings of Giordani et al and Houben et al as referenced in this Office's previous actions are incorporated herein by reference in their entirety.

Applicants argue that there is no reason for one of ordinary skill in the art to select any of the functional groups to complete the makeup of the many compounds generically encompassed by Giordani et al (Remarks at page 6).

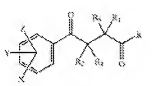
Giordani et al teach a class of 4-phenyl-4-oxobutanoic acid derivatives and their pharmaceutically acceptable salts (Abstract) with a core structure that encompasses the core structure of the present invention useful in the treatment of glaucoma/retinopathy (Col. 3, lines 4-20). Giordani et al also teach that the 4-phenyl-4-oxobutanoic acid derivatives are used as a kynurenine-3-hydroxylase inhibitor (Col. 3, limes 4-5). It is well understood in the art that retinopathy is a known complication associated with diabetes. (Houben et al, Col. 1, lines 38-67; *see also* Diabetes Research Foundation, "Diabetes and Your Eyesight," printed from http://www.glaucoma.org/learn/diabetes_and_yo.html, 2 pages).[1]

More specifically, as with the present invention, Giordani et al disclose the following

[1] Cited on previous PTO-892 form.

Accordingly, the present invention provides a 4-phenyl-4-oxo-butanoic acid derivative of formula (I) either as a single isomer or as mixture of isomers

(I)



wherein

X, Y and Z are, each independently, hydrogen, halogen, cyano, nitro, C_1–C_6 alkyl, phenyl, benzyl, C_2–C_6 alkenyl, C_2–C_6 alkynyl, C_1–C_6 alkoxy or C_1–C_6 alkylthio;

R is hydroxy; —OR_x, in which R_x is C_1–C_6 alkyl, phenyl, benzyl, C_2–C_6 alkenyl or C_2–C_6 alkynyl; —$N(R_y)_2$ or —NR_yOR_z in which each R_y is, independently, hydrogen, C_1–C_6 alkyl, C_2–C_6 alkenyl, C_2–C_6 alkynyl, phenyl or benzyl;

R_1, R_2, R_3 and R_4 are, each independently, hydrogen, halogen, hydroxy, thiol, C_1–C_6 alkoxy, C_2–C_6 alkylthio, C_1–C_6 alkyl, C_2–C_6 alkenyl, phenyl or benzyl, or

R_2 and R_3 or R_3 and R_4 together form a group =CHR_6 in which R_6 is hydrogen, a straight C_1–C_6 alkyl chain or phenyl;

(Col. 2, lines 38-67) and

As noted prior, in the present invention, R^1 may represent a heterocyclic radical, which could be identical to the phenyl ring disclosed in Goirdani et al. The present invention's R^2 is the equivalent of Giordani's R^2, and the present invention's R^3 is the equivalent of Girodani's R^4. According to Giordani, both its R^2 and R^4, just as its R^3 and R^1, can be hydrogen, halogen, thiol, alkenyl, alkoxy, etc., just as the present invention's R^2 and R^3 positions can be the same. The present invention's W represents a divalent radical which is the equivalent to the cycloalkyl formed in Giordani et al that includes R^1 and R^3, and finally, R^4 in the present invention, which is the equivalent of R in Giordani et al, can both be, for example, a heterocyclic ring or an alkenyl or alkyl.

By Applicants' own admission, Giordani et al recites thiol as one of its many options for R_1 through R_4 and correctly rectites "thiol" as a RSH with any R group attached to the S group. However, Applicants' go on to argue that aside from the aforementioned, "not a single compound with a thiol group is taught in the disclosure of the reference" (Argument of 01 December 2008 at page 4) and as a result, the instant invention is unobvious. The latter does not foreclose the relevance of the former. Giordani et al, not matter how broad, does disclose thiol. Further, giving Giordani et al its broadest reasonable interpretation, where thiol is defined as RSH, one can then contemplate an alkylthio,[2] of which a hexylthio, such as 2-cyclohexylthio … are reasonable considerations, bringing the instant claims within the purview of prior art.

With regard to there being no motivation by the skilled artisan to select a thiol of for that matter a hexylthio, the Examiner disagrees. The instant claim set is directed to a treatment methodology for diabetes. It is well understood in the pharmaceutical art that cyclic structures increase solubility and bioavailability of compounds used for consumption, providing more than ample motivation for the modification to arrive at the instant invention.

In light of the foregoing, it would have been *prima facie* obvious to one of ordinary skill in the art to utilize the administration of a 4-phenyl-4-oxobutanoic acid derivatives used as a kynurenine-3-hydroxylase inhibitor as a method of treating diabetes and associated complications.

[2] It is known and accepted in the art that alkylthio can include such examples as methylthio, ethylthio, butylthio and hexylthio, etc. Please see U.S. Patent Pregrant Publication No. 2009/0076006.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alicia Hughes whose telephone number is 571-272-6026. The examiner can normally be reached from 9:00 AM to 5:00 PM, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, can be reached at 571-272-0718. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR of Public PAIR. Status information for unpublished applications is available through Public PAIR only. For information about the PAIR system, see http://pair-direct-uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Raymond J Henley III/

Primary Examiner, Art Unit 1614